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PAPER NO. 15

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07/330,446 D.Jacobson
Yoshimura et al. Filed 3/30/89

"Human Derived Monocyte Attracting Purified Protein Product useful in a Method of Treating Infection and Neoplasms in a Human Body, and the Cloning of Full Length cDNA thereof"

Before the Board of Appeals

94-0757

Gerald M. Murphy, Jr.
for Appellant

Examiner's Answer

Mailed
1-11-93

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed 10/13/92.

(1) Status of claims.

The statement of the status of claims contained in the brief is correct.

(2) Status of Amendments After Final.

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(3) Summary of invention.

The summary of the invention contained in the brief is correct.

(4) Issues.

The appellant's statement of the issues in the brief is correct. The previous rejection of claim 9 under 35 U.S.C 112, second paragraph, is withdrawn in view of appellants' amendment.

(5) Grouping of claims.

Appellant's brief includes a statement that claims 9 and 11-19 do not stand or fall together and provides reasons as set forth in 37 CFR.1.192(c)(5) and (c)(6). The appellant's statement in the brief that certain claims do not stand or fall together is not agreed with because the claims are directed to the cDNA encoding a particular protein, expression vectors and host cells, and methods of producing said protein. Claims 11-19 depend upon claim 9, which is drawn to the cDNA encoding a monocyte chemo-attractant peptide. If said nucleotide sequence is patentable, then vectors, host cells, and methods of use are patentable also. On the contrary, if the cDNA is not found to be patentable, then claims in which the patentable feature is the DNA of interest are also not patentable. In other words, if the nucleic acid is not deemed to be patentable, then claims drawn to commonly used vectors and host cells containing said DNA and methods for use thereof to produce the protein encoded by said DNA are not patentable.

(6) Claims appealed.

A substantially correct copy of appealed claim 14 appears on page ii of the appendix to the appellant's brief. The minor errors are as follows: Claim 14 should read, "The vector of claim 13, which is LAMBDA ZAP II." See paper no. 8, page 3.

(7) Prior Art of record.

Valente, A.J. et al., "Purification of a monocyte chemotactic factor secreted by nonhuman primate vascular cells in culture," Biochemistry, vol. 27, pages 4162-4168. (1988)

(8) New prior art.

No new prior art has been applied in this examiner's answer.

(9) Grounds of rejection.

The following ground of rejection is applicable to the appealed claims:

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to the human monocyte chemoattractant peptide disclosed by appellants and the nucleotide and amino acid sequences thereof. See MPEP 706.03(n) and 706.03(z).

This rejection is necessitated by appellants' amendment. Claim 10, which was cancelled in paper no. 10, recites, "The cDNA of claim 9, wherein a mutation or variation in said cDNA occurs." Claim 10 was previously rejected under 35 U.S.C. 112, first paragraph (see paper no. 7, page 6). Claim 9, as amended, is now drawn to the substance of claim 10 and the rejection is deemed proper.

Claim 9 is drawn to the cDNA encoding a human monocyte chemo-attractant peptide or "a mutation or variation thereof". Claim 9 thus reads on and includes any type of mutation that may occur within the disclosed cDNA sequence, i.e. any insertional mutation, deletion mutation, rearrangement, or point mutation. The claim also reads on any allelic variation which may occur, including other peptides that belong to the same family of chemoattractant peptides, but which are not disclosed by appellants. The specification describes the isolation and purification of four proteins, namely GDCF-1, GDCF-2, LDCF-1, and LDCF-2. The specification also

discloses the amino acid and DNA sequences of GDCF-1 (also named MCP-1). Due to the breadth of claim 9 and the lack of guidance provided by the specification concerning identification of other chemoattractant peptides, it would require undue experimentation to determine all of the possible proteins that are included by claim 9. Claim 9 is thus deemed to be beyond the scope of the enabled invention.

Claims 9 and 11-19 are rejected under 35 U.S.C. 103 as being unpatentable over Valente et al.

Valente et al. disclose purification of a protein that has a molecular weight of approximately 15 kDa (as measured by SDS-PAGE), a basic pI, and which possesses chemotactic activity for human monocytic cells. Appellants' claimed MCP-1 possesses a molecular mass of approximately 15 kDa as measured by SDS-PAGE, a "high pI" (page 29, lines 11-12), and possesses monocytic chemotactic activity. The reference thus appears to describe the same protein as appellants.

It would have been obvious to one of ordinary skill in the art to determine the amino acid sequence of the chemotactic factor described by Valente et al., to obtain its DNA sequence, and to further clone and express this factor. At the time the invention was made, techniques for sequencing proteins were well-known in the art and it would have been within the purview of such an artisan to determine the sequence of said chemotactic factor, to further determine its nucleic acid sequence, and to clone the gene encoding said chemotactic peptide. In fact, based upon the technology at the time the invention was made, such an artisan would have expected to be able to determine the sequence of the Valente et al. protein and to clone and express it. The motivation for obtaining the amino acid and nucleotide sequences would have been for further characterization of its biologic roles and therapeutic applications.

(10) New ground of rejection.

This Examiner's Answer does not contain any new ground of rejection.

(11) Response to argument.

Appellants traverse the previous 35 U.S.C. 112, first paragraph, rejection of claim 9 on the grounds that the amendments to claim 9 limit the cDNAs encompassed by the claim, such that the claim is fully enabled by the disclosure. Appellants assert that methods for making variant nucleotide sequences are well known in the art and that a definite test of chemo-attractant activity is disclosed. Therefore, one of skill in the art would consider "mutations or variants" thereof enabled by the disclosure. These arguments have been fully considered but are not deemed to be persuasive.

The specification discloses the isolation of GDCF-1, GDCF-2, LDCF-1, and LDCF-2 and the sequence of GDCF-2 (MCP-1), but does not disclose the isolation of nor the sequence of other peptides possessing monocyte chemoattractant peptides. As now written, claim 9 reads on any type of mutant or variant form of the peptide, including any insertion, deletion, rearrangement, point mutation, or allelic variation. The specification does not disclose any mutant or variant forms of appellants' MCP, nor does the specification provide any guidance concerning the determination of other monocytic chemotactic peptides, other than those disclosed. Due to the unpredictable nature of the art, it would require undue experimentation to identify and isolate other monocyte chemoattractant peptides and to determine mutations or variations thereof that result in functional proteins. Claim 9 is deemed to be beyond the scope of the enabled invention.

In addition, appellants traverse the 35 U.S.C 103 rejection of claims 9 and 11-19 over Valente et al. on the grounds that because two different materials possess chemotactic activity does not provide a basis to conclude that such materials are obvious over each other (Appeal Brief, p. 10-11). In addition, appellants assert that the protein described by Valente et al. had an estimated molecular weight of 14,500 Da, which is different from appellants' protein that has an estimated molecular mass of about 8,400 Da. Appellants further argue that the amino acid composition of appellants' peptide is clearly distinct from the Valente et al. peptide. These arguments have been fully considered but are not deemed to be persuasive for the following reasons.

As pointed out above Valente et al. describe a protein that has a molecular mass of approximately 15 kDa, as determined by SDS-PAGE. Appellants disclose four proteins (GDCF-1, GDCF-2, LDCF-1, and LDCF-2) that have a molecular mass of approximately 15 kDa, as determined by SDS-PAGE. (see page 21, lines 6-8, and page 28). Thus, the molecular weight of appellants' protein and the Valente et al. protein is the same. The minimal molecular mass of appellants' proteins, based upon amino acid composition (which is different from the SDS-PAGE method used above), was 8400 Da. Appellants' assertions that the Valente et al. peptide is distinct from the peptides disclosed by the present application based on molecular weight, is in essence, a comparison of apples to oranges. Appellants argue that their protein is distinct based upon one method of measurement, when in fact the specification teaches that using the same method of measurement as Valente et al., the proteins are the same weight.

It is further noted that the specification teaches that discrepancies between the weight of a protein as determined by SDS-PAGE and based upon the amino acid composition have been noted by others. See page 23, lines 4-7, and page 31, line 15, through page 32, line 2. In view of this the discrepancies noted above and by appellants are not surprising.

Appellants further assert that the amino acid composition of the Valente et al. protein is clearly different from the amino acid composition of appellants' peptide. In light of the above discussion regarding the size of the molecules, it is noted that the amino acid compositions provided by Valente et al. and the Yoshimura et al. reference are based upon different molecular weights. Valente et al. is calculated assuming that the molecular weight of the chemotactic factor is 14,500 Da. Yoshimura et al., J. Immunol. 142:1956-1962, which describes appellants' work, (Table II, as referred to by appellants) is calculated assuming that that molecular weight is 8400 Da. The amino acid compositions are different because the calculations are preformed assuming different molecular weights. Amino acid compositions are calculated as amino acid residues per protein molecule. Therefore, one would expect calculations done assuming a particular molecule weighs 14,500 Da to be different from calculations performed assuming the weight is 8400 Da. Again, appellants are comparing apples to oranges. In fact, the specification teaches, "The amino acid composition of a monocyte chemo-attractant produced by aortic smooth muscle cells of the baboon [Valente et al.] is identical to that of MCP-1 as determined in Example III herein." The specification further teaches that the MCP-1 cDNA probe hybridized with baboon DNA, thus showing evidence for the relationship between MCP-1 and the smooth muscle product. See page 45, lines 8-16. Again referring to Yoshimura et al., the reference teaches that the protein described by Valente et al. is similar to appellants' GDCF and LDCF. The reference states, "If we assume that the peptide [described by Valente et al.], like LDCF, has a molecular mass of approximately half the value estimated from SDS-PAGE....the amino acid composition is similar to that of LDCF." (page 1960, second column) As suggested by Yoshimura et al., the actual molecular weight of the Valente et al. peptide and its amino acid composition, is similar to that of appellants' peptide.

Therefore, it is deemed that the protein described by Valente et al. is identical to appellants' MCP-1 and it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the amino acid and nucleotide sequences and to clone and express the gene encoding MCP-1.

CONCLUSION

For the above reasons, it is respectfully submitted that the above rejections of claims 9 and 11-19 in the application is correct and proper and that the rejections should be sustained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Dian C. Jacobson whose telephone number is (703) 308-0452. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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